CO-FORMULATION OF BROADLY NEUTRALIZING ANTIBODIES 3BNC117 AND PGT121: ANALYTICAL CHALLENGES DURING PRE-FORMULATION CHARACTERIZATION AND STORAGE STABILITY STUDIES*

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In this study, we investigated analytical challenges associated with the formulation of two broadly neutralizing anti-HIV monoclonal antibodies (bnAbs), 3BNC117 and PGT121, both separately at 100 mg/mL and together at 50 mg/mL each. The bnAb formulations were characterized for relative solubility and conformational stability followed by accelerated and real-time stability studies. While the bnAbs were stable during 4°C storage, incubation at 40°C differentiated their stability profiles. Specific concentration dependent aggregation rates at 30°C and 40°C were measured by size exclusion chromatography for the individual bnAbs with the mixture showing intermediate behavior. Interestingly, while the relative ratio of the two bnAbs remained constant at 4°C, the ratio of 3BNC117 to PGT121 increased in the dimer that formed during storage at 40°C. A mass spectrometry based multi-attribute method (MAM), identified and quantified differences in modifications of the Fab regions for each bnAb within the mixture including clipping, oxidation, deamidation and isomerization sites. Each bnAb showed slight differences in the levels and sites of lysine residue glycations. Together, these data demonstrate the ability to differentiate degradation products from individual antibodies within the bnAb mixture, and that degradation rates are influenced not only by the individual bnAb concentrations but also by the mixture concentration.

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